

Appl. No. 10/027,000  
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### **REMARKS**

#### **The Invention.**

The present invention provides a novel  $\beta$ -glucosidase nucleic acid sequence, designated *bgl4*, and the corresponding BGL4 amino acid sequence. The presently claimed invention also provides expression vectors and host cells comprising a nucleic acid sequence encoding BGL4, recombinant BGL4 proteins and methods for producing the same.

#### **Status of the Application.**

Claims 2-36 are pending in the application. Applicants gratefully acknowledge that the Examiner has determined that Claims 23 and 24 are allowable.

Claims 3, 18, 21, 25 and 27-36 have been cancelled as drawn to a non-elected invention without prejudice and Applicants reserved the right to file further continuation applications on any subject matter disclosed in the instant application or on the subject matter of any previously or presently cancelled claim.

Claims 2, 6, 7 and 8 have been amended to further clarify the invention. Applicants assert new matter has not been introduced by the amendment. Support for the amendments may be found in the specification and claims as originally filed. Entry of the amendments is respectfully requested.

#### **35 U.S.C. §112, first paragraph.**

##### **Claims 2, 3-17 and 19-20**

Claims 2, 3-17 and 19-20 stand rejected under 35 USC §112, first paragraph as failing to comply with the written description requirement. Specifically, the Examiner points out that Claim 2 recites " $\beta$ -glucosidase IV endoglucanase activity" without support in the specification. The amendment dated November 20, 2003, inadvertently introduced the word "endoglucanase" into the claim. Applicants apologize for not catching the error and gratefully thank the Examiner for bringing the error to their attention. Applicants have amended Claim 2 to remove the recitation of "endoglucanase" rendering the rejection moot. Withdrawal of the rejection is respectfully requested.

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Claims 1-17, 19-20, 22 and 26

Claims 1-17, 19-20, 22 and 26 stand rejected under 35 USC §112, first paragraph as failing to enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Specifically, the Examiner asserts that it would require undue experimentation by a skilled artisan to identify regions that can be changed and make and use all the claimed variant polynucleotides. Applicants respectfully traverse.

Applicants have amended Claim 2. Thus, using a specific protocol/method for aligning sequences a person skilled in the art will be able to determine whether or not their sequence meets the identity criterium in the claims. Sequence alignment is routine in the art.

The Examiner states that "the specification does not establish: (A) a single universal method to isolate polynucleotides encoding  $\beta$ -glucosidase from any fungi; (B) a single universal method to inactivate polynucleotides encoding  $\beta$ -glucosidase from any source in any host cell; (C) regions in the polynucleotide structure which may be modified without effecting its activity of encoding a functional  $\beta$ -glucosidase; (D) the general tolerance of said polynucleotide sequence to modification and extent of such tolerance; (E) a rational and predictable scheme for modifying any nucleotide in a fungal polynucleotide with an expectation of obtaining the desired biological function; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful." See paragraph bridging pages 11 and 12 of the Office Action.

The specification need not teach one skilled in the art how to determine whether each embodiment within the scope of the claims is operable. Rather, the specification must teach how to make/or use each embodiment within the scope of the claims without undue experimentation. And, since the specification teaches how to make a beta-glucosidase (and one skilled in the art using the specification as well as the art available at the filing date of the application could determine, case by case, whether each additional embodiment, each additional beta-glucosidase, could be made and was

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operable), the specification is sufficient under 35 USC 112, first paragraph for each and every embodiment of the claimed invention.

With respect to items (A) and (B) above, there are well known methods in the art on how to isolate nucleotides encoding  $\beta$ -glucosidase or inactivate a gene. Specifically, a skilled artisan given the present  $\beta$ -glucosidase sequence would be able to employ any one of the known methods to isolate a homolog of the instant  $\beta$ -glucosidase or design a nucleotide to inactivate the  $\beta$ -glucosidase gene. In addition, the claims as currently written do not depend on the method used to isolate the nucleotide or the method to inactivate the gene.

With respect to item (C) above, Applicants note on page 24, lines 1-12, of the specification that ten sequences having the highest identity, but less than 46% identity, were all annotated as  $\beta$ -glucosidase. One skilled in the art would know how to align proteins, just as the Applicants did. Furthermore, it is well known in the art that, for example Family 3 glycosyl hydrolases have a conserved SDW motif in the catalytic domain. The present  $\beta$ -glucosidase has this motif beginning at residue 224 of Figure 2. Thus, a skilled artisan would be able to determine the conserved areas that would be less desirable to modify. Moreover, the claims require a functional  $\beta$ -glucosidase. Assays for  $\beta$ -glucosidase activity are given on, for example, page 11, lines 6-9, and page 31, lines 18-32.

Finally, with respect to items (D) – (F) above, as Applicants previously noted, there are numerous  $\beta$ -glucosidases that have lower identity than what is presently claimed. Thus, there would appear to be a large tolerance for modification to the polynucleotides. Further, Applicants provide rationale for modifying the sequence. See, for example, page 23, lines 28-30. In addition, a skilled artisan would be able to use techniques well known in the art to determine which residues would be likely candidates for modification. See, for example, US Patent 4,760,025, wherein suitable methods for manipulation of the precursor DNA sequence are disclosed; this patent granted in 1988 and is cited to show that the art relating to sequence manipulation was well known and routine at the time of filing of the instant case.

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For the reasons given above, Applicant believes the instant rejection is in error. Withdrawal of the rejection is respectfully requested.

Claim 22

Claim 22 stands rejected under 35 USC §112, first paragraph as failing to be described in the specification. Applicants have cancelled Claim 22 rendering this rejection moot. Withdrawal of the rejection is respectfully requested.

35 U.S.C. §112, second paragraph.

Claims 2, 3-17 and 19-20

Claims 2, 3-17 and 19-20 stand rejected under 35 USC §112, second paragraph as being indefinite as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner asserts that the phrase "β-glucosidase IV endoglucanase activity" is unclear. Applicants have amended Claim 2 to recite "β-glucosidase IV activity" rendering this rejection moot. Withdrawal of the rejection is respectfully requested.

In addition, Claims 2, 3-17 and 19-20 stand rejected under 35 USC §112, second paragraph as being indefinite as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner requests clarification of the recitation of "Figure 2 (SEQ ID NO:2)" in Claim 2. Applicants gratefully acknowledge the Examiner's review of the issues. In light of the Examiner's comments and upon review of the application Applicants respectfully agree with the Examiner that there is confusion. Applicants have amended Claim 2 to address the Examiner's concerns and believe that rejection is now moot. Withdrawal of the rejection is respectfully requested.

Claims 6 and 7

Claims 6 and 7 stand rejected under 35 USC §112, second paragraph as being indefinite as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner asserts that the phrase

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"derived from" is unclear. Although Applicants must respectfully disagree with the Examiner's argument and rationale, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended Claims 6 and 7 as suggested by the Examiner. Withdrawal of the rejection is respectfully requested.

Claims 8-9 and 11

Claims 8-9 and 11 stand rejected under 35 USC §112, second paragraph as being indefinite as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner asserts that the phrases "including a polynucleotide" and "including the expression construct" are unclear. Applicants have (really!) amended the claims to recite "comprising" rendering this rejection moot. Withdrawal of the rejection is respectfully requested.

35 U.S.C. §103.

Claim 22

The Examiner has rejected claim 22 as allegedly obvious over Takashima *et al.* (J. Biochem. (1999) 125:728-736) and the common knowledge in the art. Applicant respectfully traverses the rejection. However, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have cancelled Claim 22 (as noted above). Withdrawal of the rejection is respectfully requested.

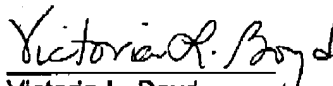
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**CONCLUSION**

In light of the above amendments, as well as the remarks, the Applicants believe the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-7615.

Respectfully submitted,

  
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